

Tom Delaval please

Access DB# 109983

SEARCH REQUEST FORM

Scientific and Technical Information Center

DEC - 8 2003

Requester's Full Name: SABINA GARCIA Examiner #: 74141 Date: 11/12/03
Art Unit: 1616 Phone Number 305-3916 Serial Number: 101069414
Mail Box and Bldg/Room Location: 2219 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Agents for the enhanced oxygen delivery
Inventors (please provide full names): Lehin Jean-Marie

Earliest Priority Filing Date: 8/25/03 1999 371 of 107/1500/22583

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number

1 CL - 11

Please search for the compounds
BGSC + BGTC, structures of steroids are
on p-18 (enclosed)
You may leave open at C-17 for
broader search, after searching
separately BGSC + BGTC

Please see attached sheets

Thank you

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Searcher: an
Searcher Phone #: 4498
Searcher Location: _____
Date Searcher Picked Up: 12/8
Date Completed: 12/8
Searcher Prep & Review Time: _____
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Type of Search

NA Sequence (#) _____

AA Sequence (#) ☒ _____

Structure (#) _____

Bibliographic _____

Litigation _____

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Patent Family _____

Other _____

Vendors and cost where applicable

STN ☒ _____

Dialog _____

Questel/Orbit _____

Dr. Link _____

Lexis/Nexis _____

Sequence Systems _____

WWW/Internet _____

Other (specify) _____

=> fil reg

FILE 'REGISTRY' ENTERED AT 16:55:58 ON 08 DEC 2003
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STRUCTURE FILE UPDATES: 7 DEC 2003 HIGHEST RN 624286-58-4
DICTIONARY FILE UPDATES: 7 DEC 2003 HIGHEST RN 624286-58-4

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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L17 STR

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NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

L19 35097 SEA FILE=REGISTRY SSS FUL L17

100.0% PROCESSED 122111 ITERATIONS

35097 ANSWERS

SEARCH TIME: 00.00.13

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L1 1 S (WO2000-US22583 OR US99-150574#)/AP, PRN
SEL RN

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L2 9 S E1-E9
L3 2 S L2 AND C5-C6-C6-C6/ES AND N/ELS
E C36H66N8O2/MF
L4 2 S E3

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      E C37H67N7O2/MF
L5      1 S E3
      SEL RN L3
L6      2 S E1-E2/CRN
L7      4 S L3,L6
L8      2 S L2 AND 46.150.1/RID
L9      284 S 83-86-3/CRN
L10     252 S L9 NOT (PMS OR IDS OR MXS)/CI
L11     134 S L10 NOT (UNSPECIFIED OR WITH OR COMPD)
L12     130 S L11 AND 1/NR
      E RR32.3.5/RID
      E 4432.3.5/RID
L13     34498 S E3
L14     STR
L15     0 S L14 CSS SAM SUB=L13
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L17     STR L14
L18     50 S L17
L19     35097 S L17 FUL
L20     10 S L13 AND L19
L21     42 S L19 AND C5-C6-C6-C6/ES
L22     32 S L21 NOT L7,L20
L23     14 S L22 NOT SQL/FA

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FILE 'HCAPLUS' ENTERED AT 16:53:27 ON 08 DEC 2003

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      E LEHN J/AU
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      E NICOLAU Y/AU
L27     24 S E3,E6,E7
      E GMP/PA,CS
L28     89 S E3-E39
L29     6 S L25 AND L26-L28
L30     10 S L25,L29
L31     1 S L30 AND L8
L32     1 S L30 AND L12
L33     1 S L31,L32
L34     10 S L30-L33

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FILE 'USPATFULL, USPAT2' ENTERED AT 16:55:43 ON 08 DEC 2003

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L35     5 S L7
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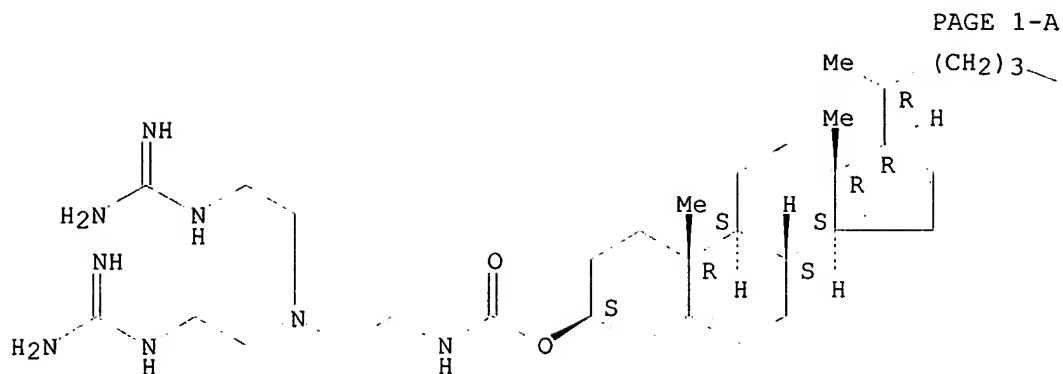
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L7      ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2003 ACS on STN
RN      182056-15-1  REGISTRY
CN      Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]ami
      no]ethyl]carbamate, dihydrochloride (9CI)  (CA INDEX NAME)
FS      STEREOSEARCH
MF      C36 H66 N8 O2 . 2 Cl H
SR      CA
LC      STN Files:  CA, CAPLUS, USPATFULL
CRN     (182056-06-0)

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Absolute stereochemistry.



● 2 HCl

PAGE 1-B

CHMe₂

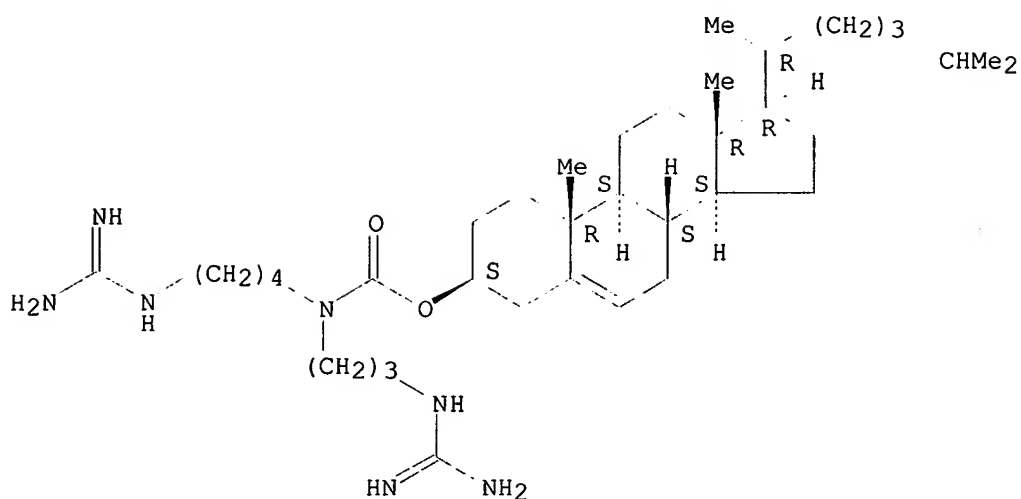
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:234484

REFERENCE 2: 125:239451

L7 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 182056-12-8 REGISTRY
CN Cholest-5-en-3-ol (3 β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H67 N7 O2 . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (182055-89-6)

Absolute stereochemistry.



● 2 HCl

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

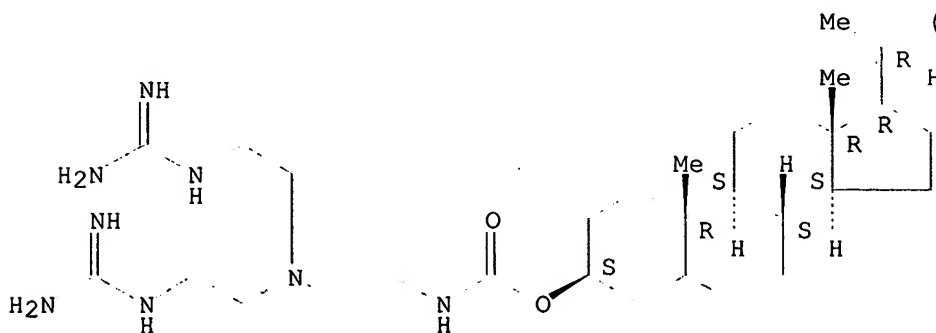
REFERENCE 1: 127:234484

REFERENCE 2: 125:239451

L7 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 182056-06-0 REGISTRY
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FS STEREOSEARCH
MF C36 H66 N8 O2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

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PAGE 1-B

CHMe2

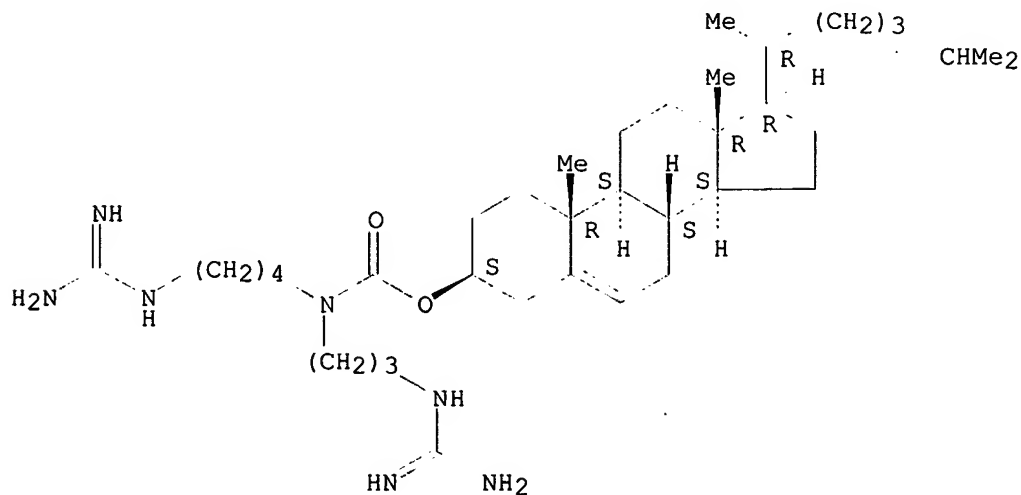
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9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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REFERENCE 2: 137:389091
REFERENCE 3: 136:319345
REFERENCE 4: 134:212794
REFERENCE 5: 131:106801
REFERENCE 6: 131:54460
REFERENCE 7: 130:57047
REFERENCE 8: 126:258428
REFERENCE 9: 125:239451

L7 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 182055-89-6 REGISTRY
CN Cholest-5-en-3-ol (3 β)-, [4-[(aminoiminomethyl)amino]butyl][3-
[(aminoiminomethyl)amino]propyl]carbamate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H67 N7 O2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:212794

REFERENCE 2: 125:239451

=> fil uspatall

FILE 'USPATFULL' ENTERED AT 16:56:21 ON 08 DEC 2003

CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 16:56:21 ON 08 DEC 2003

CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr tot 135

L35 ANSWER 1 OF 5 USPATFULL on STN

AN 2002:88021 USPATFULL

TI Stabilization of lipid:DNA formulations during nebulization

IN Densmore, Jr., Charles L., The Woodlands, TX, United States

Knight, J. Vernon, Houston, TX, United States

Waldrep, J. Clifford, The Woodlands, TX, United States

Kinsey, Berma M., Houston, TX, United States

PA Research Development Foundation, Carson City, NV, United States (U.S. corporation)

PI US 6375980 B1 20020423

AI US 1999-356635 19990719 (9)

RLI Continuation-in-part of Ser. No. US 1999-227648, filed on 8 Jan 1999, now patented, Pat. No. US 6106859, issued on 22 Aug 2000

PRAI US 1998-71052P 19980108 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Schwartzman, Robert A.; Assistant Examiner: Schnizer, Richard

LREP Adler, Benjamin Aaron

CLMN Number of Claims: 9

ECL Exemplary Claim: 4

DRWN 22 Drawing Figure(s); 22 Drawing Page(s)

LN.CNT 1140

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, a neutral co-lipid; and tryptone. Also provided is a nebulized cationic lipid: neutral co-lipid: DNA suspension useful for lipid-DNA transfections, wherein the cationic lipid is bis(guanidinium)-tren-cholesterol and the neutral co-lipid is dioleoylphosphatidylethanolamine (DOPE).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

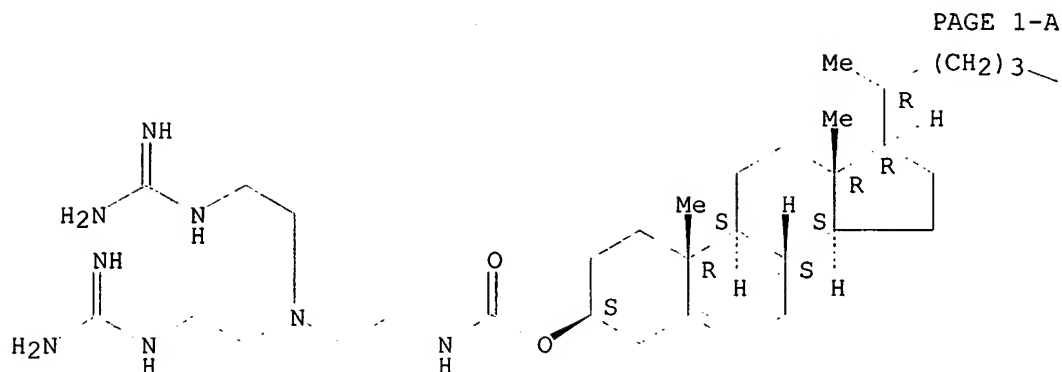
IT 182056-06-0

(liposomes containing; stabilization of lipid:DNA formulations during nebulization)

RN 182056-06-0 USPATFULL

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CHMe₂

L35 ANSWER 2 OF 5 USPATFULL on STN
 AN 2001:202605 USPATFULL
 TI Compounds related to the amidinium family, pharmaceutical compositions containing same, and uses thereof
 IN Lehn, Jean-Marie, Strasbourg, France
 Lehn, Pierre, Paris, France
 Vigneron, Jean-Pierre, Boissy-sur-Saint-Yon, France
 PA Centre National de la Recherche Scientifique, Paris, France (non-U.S. corporation)
 PI US 6316422 B1 20011113
 AI US 2000-706619 20001106 (9)
 RLI Continuation of Ser. No. US 125825, now patented, Pat. No. US 6143729
 PRAI FR 1996-2604 19960301
 FR 1996-9557 19960730
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: LeGuyader, John L.; Assistant Examiner: Epps, Janet L.
 LREP Synnestvedt & Lechner LLP
 CLMN Number of Claims: 14
 ECL Exemplary Claim: 1
 DRWN 16 Drawing Figure(s); 8 Drawing Page(s)
 LN.CNT 959

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel amidinium derivatives of formula (I), wherein R₁ is a cholesterol derivative or an alkylamino-NR'R" grouping, and each of R₂ and R₃ is independently a hydrogen atom or a grouping of formula (II), wherein each of R₄ and R₅ is independently a hydrogen atom or a grouping of formula (III), are disclosed. The corresponding pharmaceutical compositions, which are particularly useful in gene therapy for transferring therapeutic genes into cells, are also disclosed. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

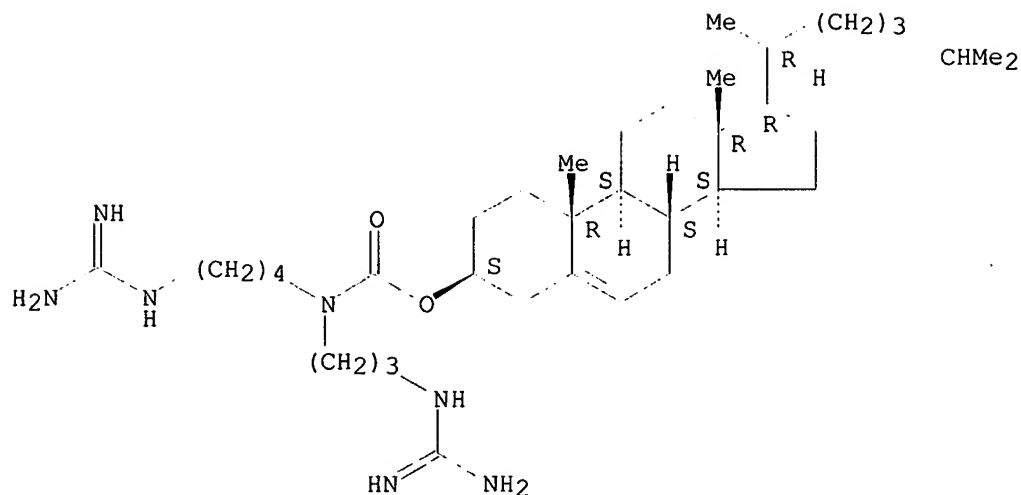
IT 182056-12-8P 182056-15-1P

(preparation of compds. related to the amidinium family and their uses in gene therapy)

RN 182056-12-8 USPATFULL

CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

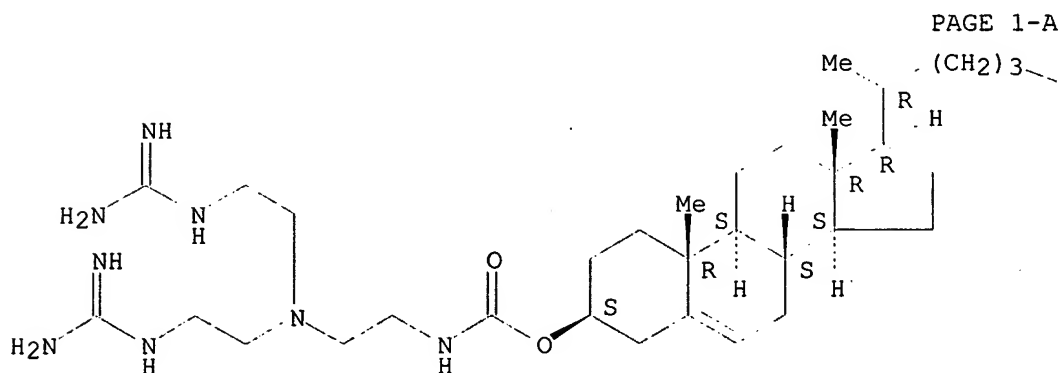
Absolute stereochemistry.



● 2 HCl

RN 182056-15-1 USPATFULL
 CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

PAGE 1-B

CHMe2

L35 ANSWER 3 OF 5 USPATFULL on STN
 AN 2001:168815 USPATFULL
 TI Alignment mechanism for computer system having a portable computer and

docking station
 IN Helot, Jacques H., San Mateo, CA, United States
 PA Hewlett-Packard Company, Palo Alto, CA, United States (U.S. corporation)
 PI US 6297953 B1 20011002
 AI US 1998-71052 19980430 (9)
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: Picard, Leo P.; Assistant Examiner: Lea-Edmonds, Lisa
 LREP Rose, Curtis G.
 CLMN Number of Claims: 6
 ECL Exemplary Claim: 1
 DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
 LN.CNT 350

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A computer system has a docking station and a portable computer. The docking station has a platform and a housing having a docking connector. The platform has one or more elevated rails. The portable computer has a computer connector, a base unit having a top portion and a bottom portion, a display unit connected to the top portion of said base unit, and one or more recessed grooves on the bottom portion of the base unit. The elevated rail or rails on the docking station interact with the recessed groove or grooves on the portable computer to guide the portable computer into a proper alignment with the housing of the docking station when the portable computer is placed on the platform and slid towards the housing so that the computer connector lines up with and connects to the docking connector. The docking station platform may have side walls or rotatable bumpers on the sides of the platform to provide coarse alignment between the docking station and the portable computer, and to prevent the portable computer from sliding off the platform during the alignment process. Preferably, the recessed groove or grooves are flared at the back edge of the portable computer to further assist in the alignment of the portable computer with the docking station. The docking station of the preferred and alternate embodiments of the invention can accommodate portable computers of different form factors and thus do not need to be replaced each time a new model of a personal computer is released with a different form factor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

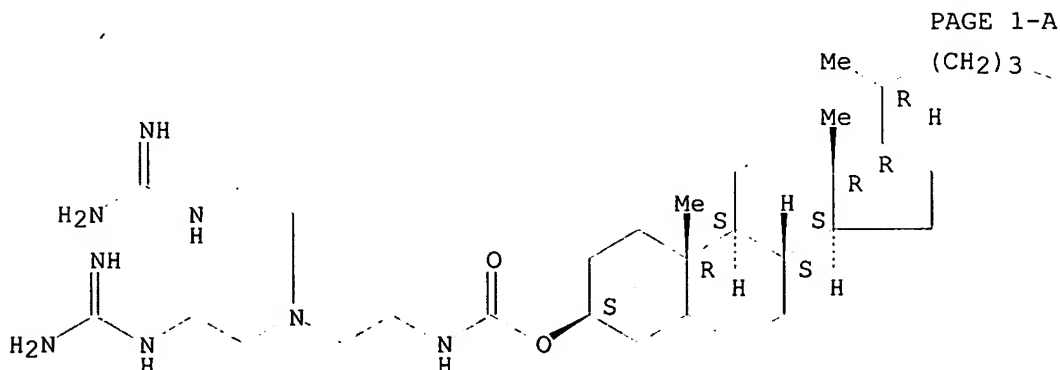
IT 182056-06-0

(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

RN 182056-06-0 USPATFULL

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe2

L35 ANSWER 4 OF 5 USPATFULL on STN
AN 2000:150149 USPATFULL
TI Compounds related to the amidinium family, pharmaceutical compositions
containing same, and uses thereof
IN Lehn, Jean-Marie, Strasbourg, France
Lehn, Pierre, Paris, France
Vigneron, Jean-Pierre, Boissy-sur-Saint-Yon, France
PA Aventis Pharma S.A., Antony, France (non-U.S. corporation)
PI US 6143729 20001107
WO 9731935 19970904
AI US 1998-125825 19980911 (9)
WO 1997-FR364 19970228
19980911 PCT 371 date
19980911 PCT 102(e) date

PRAI FR 1996-2604 19960301
FR 1996-9557 19960730

DT Utility
FS Granted

EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Epps, Janet

LREP Synnestvedt & Lechner LLP

CLMN Number of Claims: 32

ECL Exemplary Claim: 1

DRWN 16 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 1044

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel amidinium derivatives of formula (I), wherein R1 is a cholesterol derivative or an alkylamino-NR'R" grouping, and each of R2 and R3 is independently a hydrogen atom or a grouping of formula (II), wherein each of R4 and R5 is independently a hydrogen atom or a grouping of formula (III), are disclosed. The corresponding pharmaceutical compositions, which are particularly useful in gene therapy for transferring therapeutic genes into cells, are also disclosed. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

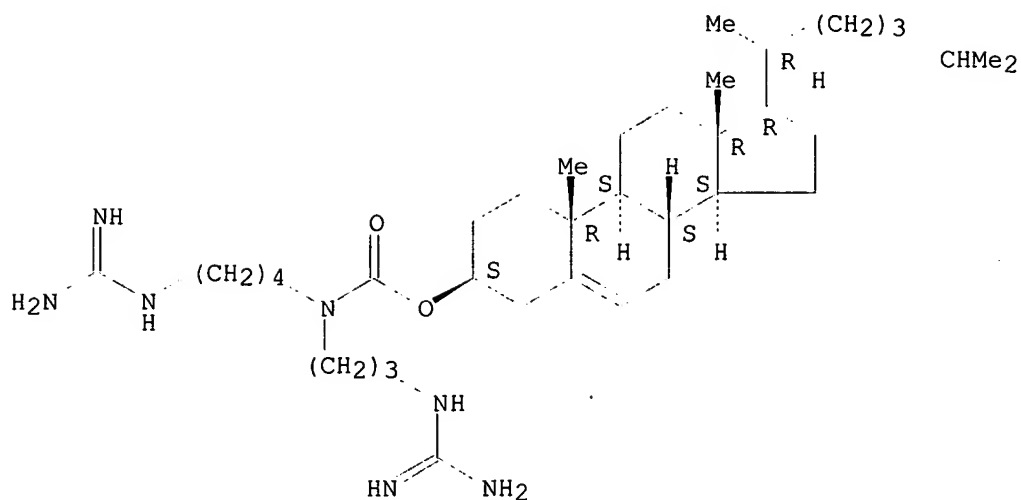
IT 182056-12-8P 182056-15-1P

(preparation of compds. related to the amidinium family and their uses in gene therapy)

RN 182056-12-8 USPATFULL

CN Cholest-5-en-3-ol (3 β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

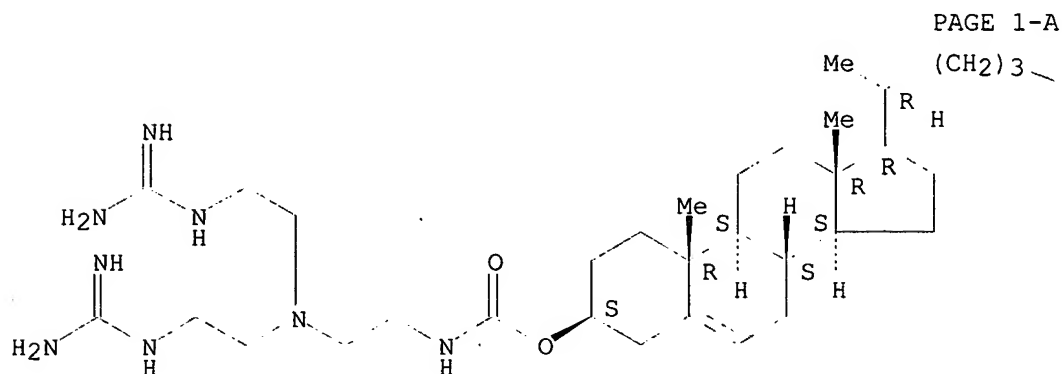


● 2 HCl

RN 182056-15-1 USPATFULL

CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

PAGE 1-B

CHMe₂

L35 ANSWER 5 OF 5 USPATFULL on STN

AN 2000:109365 USPATFULL

TI Stabilization of lipid:DNA formulations during nebulization

IN Densmore, Jr., Charles L., 83 S. Copper Sage Cr., The Woodlands, TX,
United States 77381

Knight, J. Vernon, 29 Lana La., Houston, TX, United States 77027
 Waldrep, J. Clifford, 6 Wind Trace Ct., The Woodlands, TX, United States 77381

Kinsey, Berma M., 3702 Elmore St., Houston, TX, United States 77005

PI US 6106859 20000822
 AI US 1999-227648 19990108 (9)
 PRAI US 1998-71052P 19980108 (60)
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Campell, Bruce R.; Assistant Examiner: Schnizer, Richard
 LREP Adler, Benjamin Aaron
 CLMN Number of Claims: 3
 ECL Exemplary Claim: 1
 DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
 LN.CNT 475

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, (c) a neutral co-lipid; and (d) tryptone. Also provided is a nebulized cationic lipid:DNA suspension useful for lipid-DNA transfections, wherein said cationic lipid is bis(guanidinium)-tren-cholesterol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

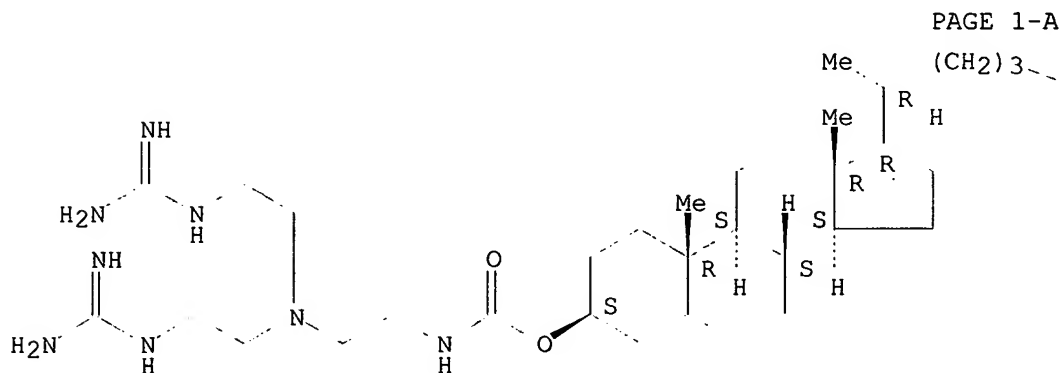
IT 182056-06-0

(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

RN 182056-06-0 USPATFULL

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe₂

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 16:56:43 ON 08 DEC 2003

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FILE COVERS 1907 - 8 Dec 2003 VOL 139 ISS 24
FILE LAST UPDATED: 7 Dec 2003 (20031207/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 134

L34 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:399692 HCAPLUS
DN 139:255843
ED Entered STN: 27 May 2003
TI Gene therapy for hepatocellular carcinoma using non-viral vectors composed of bis guanidinium-tren-cholesterol and plasmids encoding the tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3
AU Tran, Phuong-Lan; Vigneron, Jean-Pierre; Pericat, David; Dubois, Sylvie; Cazals, Dominique; Hervy, Martial; DeClerck, Yves A.; Degott, Claude; Auclair, Christian
CS LBPA, CNRS-UMR 8532, Ecole Normale Supérieure, Cachan, 94235, Fr.
SO Cancer Gene Therapy (2003), 10(6), 435-444
CODEN: CGTHEG; ISSN: 0929-1903
PB Nature Publishing Group
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 1, 14
AB Metalloproteinases (MMPs) and their natural inhibitors (TIMPs) contribute to the regulation of tumor microenvironment. Their expressions are deregulated in almost all human cancers. We report a novel approach to gene therapy of hepatocellular carcinoma (HCC), using repeated injections of DNA plasmids encoding the tissue inhibitors of metalloproteinases (TIMPs) TIMP-2 or TIMP-3, and a novel competent formulation of gene transfer based on nontoxic cationic cholesterol derivs. The new gene delivery system was efficient in demonstrating the antitumor efficiency of TIMP-2 or TIMP-3 in inhibiting tumor growth of human HuH7 HCC cells xenografted into nude mice. We show, for the first time, an in vivo effect of TIMP-3 in delaying HCC tumor growth. No treatment-related toxicity was noted. An inhibition of angiogenesis and tumor necrosis accompanied the inhibitory effects of TIMP-2 or TIMP-3 on tumor expansion and invasion. We also report a bystander effect produced by transfected HuH7 tumor cells mixed with untransfected cells in 1:1 ratio in culture that resulted in killing 98% of cells within 96 h. In addition, the soluble forms of TIMP-2 and TIMP-3 expressed by transfected cells exerted a cytotoxic effect on untransfected HuH7 cell cultures. Taken together, these results demonstrate the potential efficacy of repeated treatment of secreted TIMP-2 and TIMP-3 for the design of nonviral gene therapy for hepatocarcinoma.
ST gene therapy hepatocellular carcinoma lipoplex vector TIMP2 TIMP3; tissue inhibitor metalloproteinase gene therapy hepatocarcinoma; bis guanidinium tren cholesterol lipoplex vector
IT Antitumor agents

Gene therapy

Plasmid vectors

(gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT Human

Mouse

(gene therapy of human hepatocellular carcinoma xenografted in athymic mice)

IT Liver, neoplasm

(hepatoma; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT Drug delivery systems

(liposomes; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT Transduction, genetic

(with BGTC vectors; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT 124861-55-8, Tissue inhibitor metalloproteinase-2 145809-21-8, Tissue inhibitor of metalloproteinase-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gene for; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT 182056-06-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Ahonen, M; Cancer Res 1998, V58, P2310 HCAPLUS
- (2) Ahonen, M; Mol Ther 2002, V5, P705 HCAPLUS
- (3) Amour, A; FEBS Lett 1998, V435, P39 HCAPLUS
- (4) Amour, A; FEBS Lett 2000, V473, P275 HCAPLUS
- (5) Anderson, S; Clin Cancer Res 1998, V4, P1649 HCAPLUS
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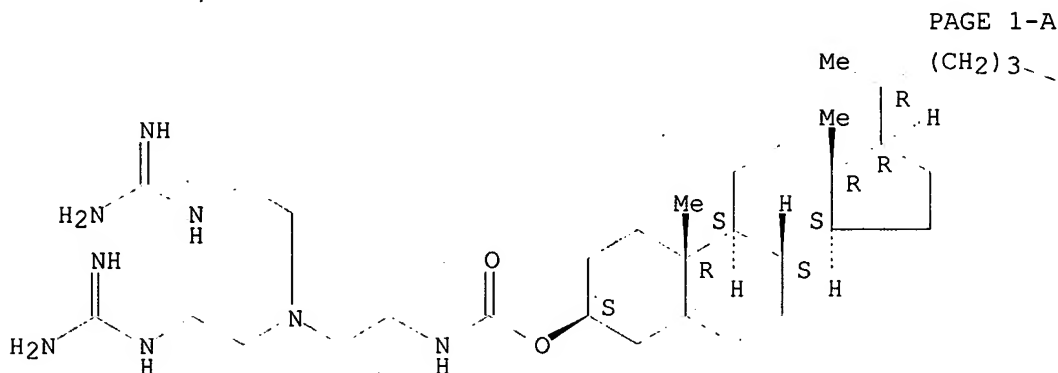
IT 182056-06-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex
 vectors and plasmids encoding tissue inhibitors of metalloproteinases
 TIMP-2 and TIMP-3)

RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]ami
 no]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

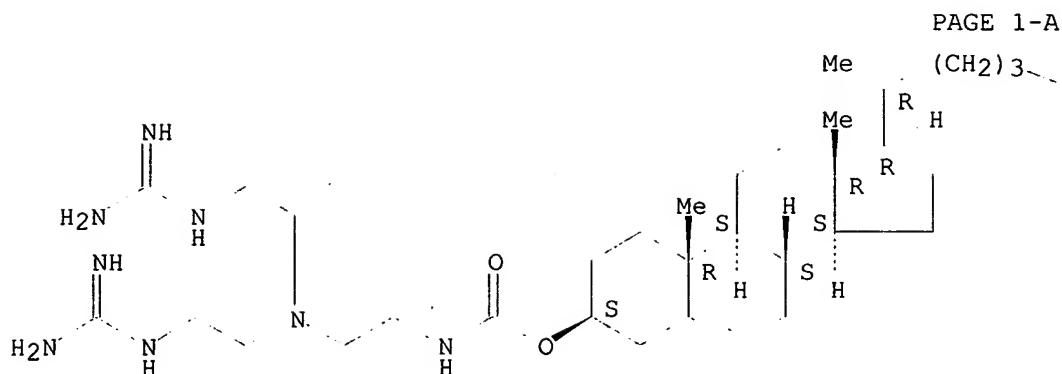


CHMe₂

L34 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
 AN 2002:311301 HCAPLUS
 DN 137:389091
 ED Entered STN: 25 Apr 2002
 TI Various cationic carriers for in vitro transfection of tumor and
 endothelial cell lines
 AU Zemlinska, Barbara; Sochanik, Aleksander; Missol-Kolka, Ewa; Szala,
 Stanislaw
 CS Department of Molecular Biology, Center of Oncology-Maria Sklodowska-Curie
 Memorial Institute, Gliwice, 44-101, Pol.
 SO Acta Biochimica Polonica (2002), 49(1), 285-290
 CODEN: ABPLAF; ISSN: 0001-527X
 PB Polish Biochemical Society
 DT Journal

LA English
 CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 3
 AB We compared the efficiency of in vitro DNA transfer into selected tumor and endothelial cell lines using complexes of plasmid DNA and cationic carriers: DDAB/DOPE, DC-Chol/DOPE, Arg-Chol/DOPE, Gly-Chol/DOPE, Arg-Gly-Chol/DOPE, BGTC/DOPE, and PEI. The best carriers for transfecting the majority of tested cells lines at optimized carrier-to-DNA weight ratios were PEI and BGTC/DOPE.
 ST tumor endothelium transfection plasmid DNA cationic carrier
 IT Bladder, neoplasm
 (carcinoma; cationic carriers for transfection of tumor and endothelial cell lines)
 IT Genetic vectors
 Human
 Melanoma
 Neoplasm
 Plasmid vectors
 Transformation, genetic
 (cationic carriers for transfection of tumor and endothelial cell lines)
 IT Blood vessel
 (endothelium; cationic carriers for transfection of tumor and endothelial cell lines)
 IT 3700-67-2, Dimethyldioctadecyl ammonium bromide 4004-05-1, DOPE
 9002-98-6 73670-26-5 137056-72-5 182056-06-0 475645-85-3
 475645-86-4
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cationic carriers for transfection of tumor and endothelial cell lines)
 RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE
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 (20) Vigneron, J; Proc Natl Acad Sci USA 1996, V93, P9682 HCAPLUS
 (21) Wicks, I; Hum Gene Ther 1995, V6, P317 HCAPLUS
 IT 182056-06-0
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cationic carriers for transfection of tumor and endothelial cell lines)
 RN 182056-06-0 HCAPLUS
 CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CHMe₂

L34 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
 AN 2002:309785 HCAPLUS
 DN 136:319345
 ED Entered STN: 25 Apr 2002
 TI Stabilization of lipid:DNA formulations during nebulization
 IN Densmore, Charles L., Jr.; Knight, J. Vernon; Waldrep, J. Clifford;
 Kinsey, Berma M.
 PA Research Development Foundation, USA
 SO U.S., 33 pp., Cont.-in-part of U.S. 6,106,859.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM A16K009-127
 ICS A16K051-00; C12N015-88
 NCL 424450000
 CC 1-1 (Pharmacology)
 Section cross-reference(s): 3
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6375980	B1	20020423	US 1999-356635	19990719
	US 6106859	A	20000822	US 1999-227648	19990108
PRAI	US 1998-71052P	P	19980108		
	US 1999-227648	A2	19990108		

AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, a neutral co-lipid; and tryptone. Also provided is a nebulized cationic lipid: neutral co-lipid: DNA suspension useful for lipid-DNA transfections, wherein the cationic lipid is bis(guanidinium)-tren-cholesterol and the neutral co-lipid is dioleoylphosphatidylethanolamine (DOPE).

ST liposome nebulization cationic neutral lipid tryptone DNA gene therapy
 IT Gene, animal

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (TP53, gene therapy of lung cancer with; stabilization of lipid:DNA formulations during nebulization)

IT Lipids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cationic, liposomes containing; stabilization of lipid:DNA formulations during nebulization)

IT Cystic fibrosis
Lung, neoplasm
(gene therapy of; stabilization of lipid:DNA formulations during nebulization)

IT Phosphatidylcholines, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing egg yolk or hydrogenated soybean; stabilization of lipid:DNA formulations during nebulization)

IT Plasmid vectors
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)

IT Peptones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)

IT Drug delivery systems
(liposomes, aerosols; stabilization of lipid:DNA formulations during nebulization)

IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neutral, liposomes containing; stabilization of lipid:DNA formulations during nebulization)

IT Gene therapy
Transformation, genetic
(stabilization of lipid:DNA formulations during nebulization)

IT 63-89-8, Dipalmitoylphosphatidylcholine 4004-05-1,
Dioleoylphosphatidylethanolamine 4235-95-4 18194-24-6,
Dimyristoylphosphatidylcholine 18194-25-7, Dilauroylphosphatidylcholine
182056-06-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

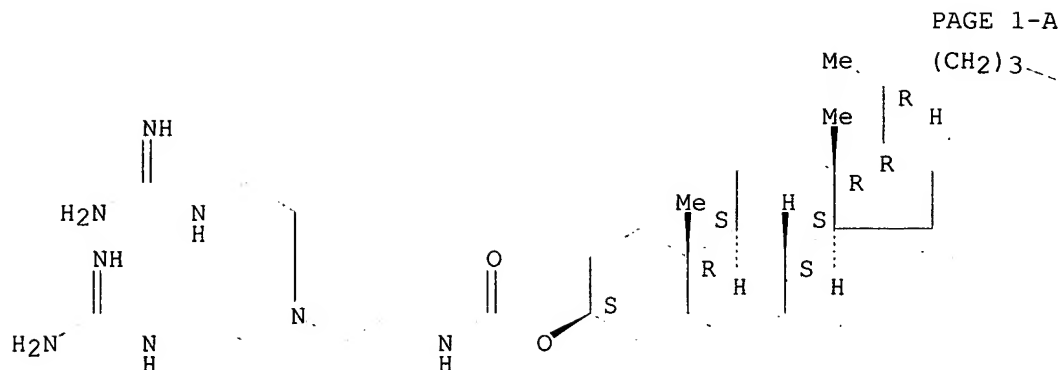
RE
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(7) Yaroush; US 5077211 A 1991 HCAPLUS

IT 182056-06-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)

RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CHMe₂

L34 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
 AN 2001:152502 HCAPLUS
 DN 134:212794
 ED Entered STN: 02 Mar 2001
 TI Enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble molecule and anionic ligand for a cellular receptor.
 IN Nicolau, Yves Claude; Lehn, Jean-Marie
 PA GMP Companies, Inc., USA
 SO PCT Int. Appl., 56 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K038-00
 CC 63-8 (Pharmaceuticals)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001013933	A2	20010301	WO 2000-US22583	20000817
	WO 2001013933	A3	20010719		
	WO 2001013933	C2	20020912		
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	EP 1223942	A2	20020724	EP 2000-957519	20000817
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL		
	JP 2003507430	T2	20030225	JP 2001-518070	20000817
PRAI	US 1999-150574P	P	19990825		
	WO 2000-US22583	W	20000817		
AB	The present invention comprises compds., compns., and methods capable of delivering a broad range of anionic mols. to the cytoplasm of mammalian cells and methods that enhance the ability of mammalian red blood cells to deliver oxygen, by delivering a ligand for the allosteric site of Hb to				

the cytoplasm of the blood cells. An example was given in which red blood cells were process with dodecasodium inositol hexaphosphate.

ST oxygen delivery Hb lipophilic ligand

IT Infection

(anaerobic; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cellular; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Alkalosis

Anemia (disease)

Hypoxia, animal

Lipophilicity

Lung, disease

(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Sterols

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Hemoglobins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Heart, disease

(failure; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Necrosis

(gangrene; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Heart, disease

(infarction; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Brain, disease

(stroke; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 83-86-3, Inositol hexaphosphate 17211-15-3,

myo-Inositol, hexakis(dihydrogen phosphate), dodecasodium salt

RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 57-88-5, Cholesterol, biological studies 182055-89-6

182056-06-0

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 7782-44-7, Oxygen, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 57-12-5, Cyanide, biological studies 630-08-0, Carbon monoxide, biological studies 10102-43-9, Nitric oxide, biological studies

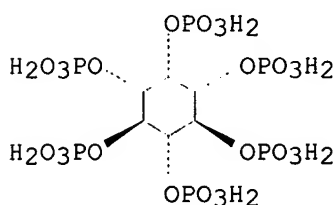
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (poisoning; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 83-86-3, Inositol hexaphosphate 17211-15-3, myo-Inositol, hexakis(dihydrogen phosphate), dodecasodium salt
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

RN 83-86-3 HCAPLUS

CN myo-Inositol, hexakis(dihydrogen phosphate) (9CI) (CA INDEX NAME)

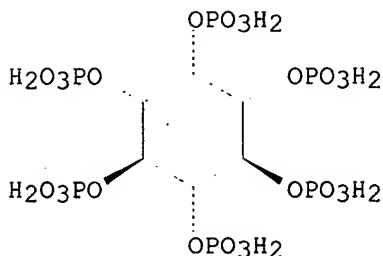
Relative stereochemistry.



RN 17211-15-3 HCAPLUS

CN myo-Inositol, hexakis(dihydrogen phosphate), dodecasodium salt (9CI) (CA INDEX NAME)

Relative stereochemistry.



●12 Na

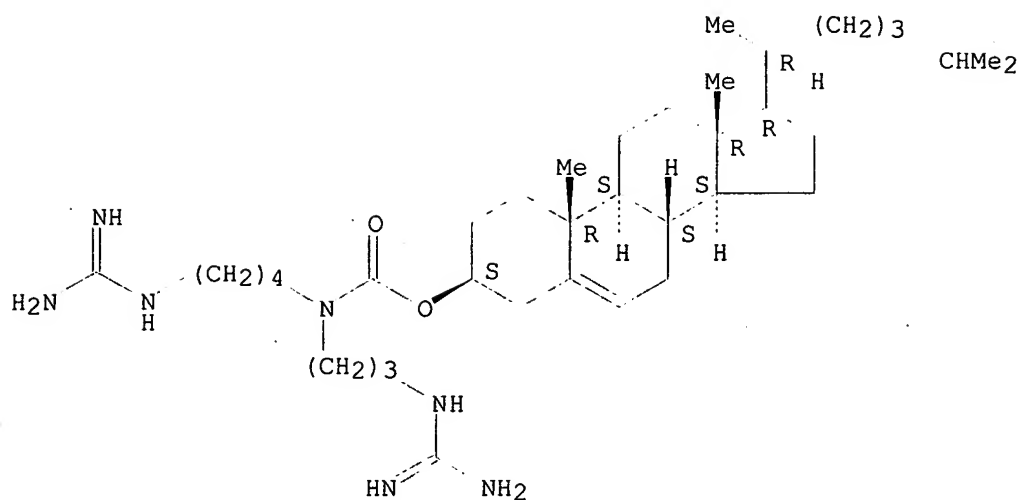
IT 182055-89-6 182056-06-0

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

RN 182055-89-6 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate (9CI) (CA INDEX NAME)

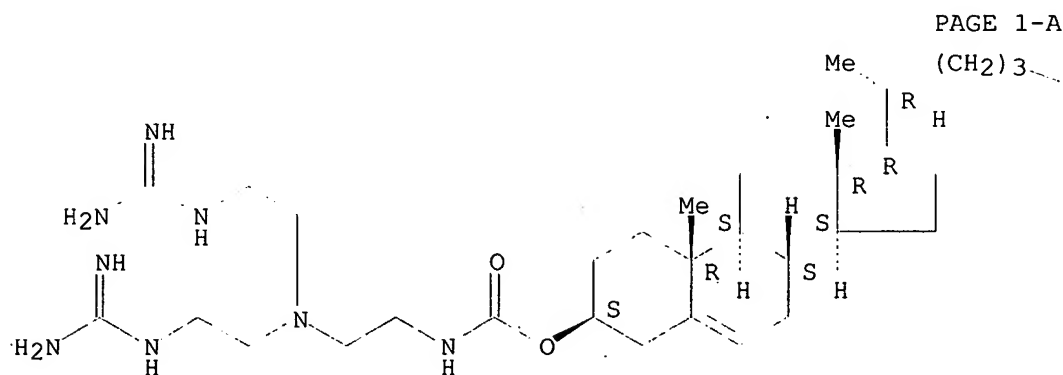
Absolute stereochemistry.



RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

PAGE 1-B

CHMe2

L34 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:449397 HCAPLUS

DN 131:106801

ED Entered STN: 22 Jul 1999

TI Stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection

IN Densmore, Charles L.; Knight, J. Vernon; Waldrep, J. Clifford; Kinsey, Berma M.

PA Research Development Foundation, USA

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K048-00
ICS C12N015-00; C12N005-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9934837	A1	19990715	WO 1999-US488	19990108
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	TW 520294	B	20030211	TW 1998-87110582	19980630
	ZA 9900097	A	20000707	ZA 1999-97	19990107
	CA 2315708	AA	19990715	CA 1999-2315708	19990108
	AU 9923141	A1	19990726	AU 1999-23141	19990108
	AU 751969	B2	20020905		
	EP 1045703	A1	20001025	EP 1999-903023	19990108
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2002500203	T2	20020108	JP 2000-527284	19990108
	RU 2213578	C2	20031010	RU 2000-120678	19990108
PRAI	US 1998-71052P	P	19980108		
	WO 1999-US488	W	19990108		
AB	The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, (c) a neutral co-lipid; and (d) tryptone. Also provided is a nebulized cationic lipid:DNA suspension useful for lipid-DNA transfections, wherein said cationic lipid is. bis(guanidinium)-tren-cholesterol.				
ST	gene therapy transfection lipid DNA formulation				
IT	Peptones				
	RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (Tryptones; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				
IT	Lipids, biological studies				
	RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (cationic; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				
IT	Drug delivery systems				
	(liposomes; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				
IT	Promoter (genetic element)				
	RL: PEP (Physical, engineering or chemical process); PROC (Process) (of cytomegalovirus; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				
IT	Cytomegalovirus				
	(promoter of; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				
IT	Phosphatidylcholines, biological studies				
	RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (soya, hydrogenated; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				
IT	Drug delivery systems				
	(sprays; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)				

IT Animal tissue culture
 Gene therapy
 Genetic vectors
 Plasmid vectors
 Stabilizing agents
 (stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Phosphatidylcholines, biological studies
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT DNA
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Escherichia coli
 (β -galactosidase reporter gene of; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Reporter gene
 RL: PEP (Physical, engineering or chemical process); PROC (Process)
 (β -galactosidase, of E. coli; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT 9031-11-2, β -Galactosidase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (reporter gene encoding, of E. coli; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT 2462-63-7, Dioleoylphosphatidylethanolamine 2644-64-6, Dipalmitoylphosphatidylcholine 18656-38-7, Dimyristoylphosphatidylcholine 18656-40-1, Dilauroylphosphatidylcholine 182056-06-0
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT 230949-32-3
 RL: PEP (Physical, engineering or chemical process); PROC (Process)
 (stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

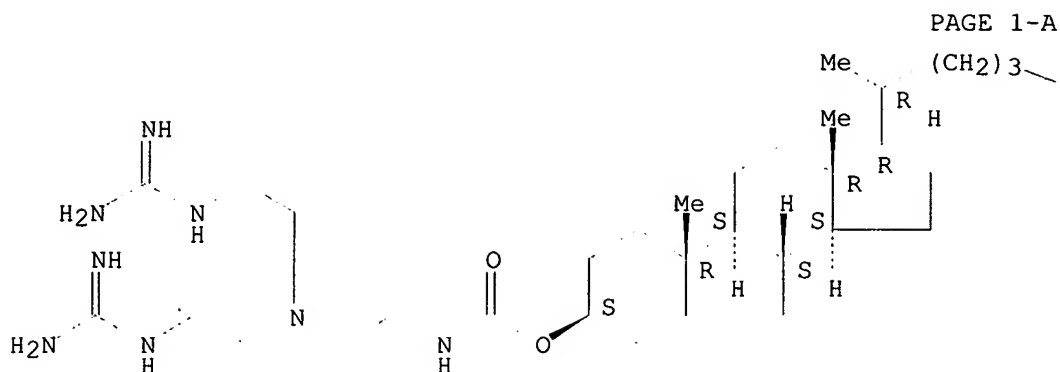
(1) Akao; J Chem Soc Perkin Trans 1997, V2(2), P213
 (2) Debs; US 5641662 A 1997 HCAPLUS
 (3) Legros; US 5211955 A 1993 HCAPLUS
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IT 182056-06-0
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CHMe₂

L34 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:198667 HCAPLUS

DN 131:54460

ED Entered STN: 29 Mar 1999

TI Structural characteristics of supramolecular assemblies formed by
guanidinium-cholesterol reagents for gene transfectionAU Pitard, Bruno; Oudrhiri, Noufissa; Vigneron, Jean-Pierre; Hauchecorne,
Michelle; Aguerre, Olivier; Toury, Renee; Airiau, Marc; Ramasawmy, Rajen;
Scherman, Daniel; Crouzet, Joel; **Lehn, Jean-Marie**; Lehn, PierreCS Unite Mixte de Recherche, 133 Rhone-Poulenc Rorer, Centre National de la
Recherche Scientifique, Vitry-sur-Seine, 94403, Fr.SO Proceedings of the National Academy of Sciences of the United States of
America (1999), 96(6), 2621-2626

CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 9

AB We have recently discovered that cationic cholesterol derivs.
characterized by guanidinium polar headgroups are very efficient for gene
transfection in vitro and in vivo. In spite of being based on some
rationale at the mol. level, the development of these new synthetic
vectors was nevertheless empirical. Indeed, the factors and processes
underlying cationic lipid-mediated gene transfer are still poorly
understood. Thus, to get a better insight into the mechanisms involved,
we have examined the supramol. structure of lipid/DNA aggregates obtained
when using reagent bis(guanidinium)-tren-cholesterol (BGTC), either alone
or as a liposomal formulation with the neutral phospholipid dioleoyl
phosphatidylethanolamine (DOPE). We here report the results of
cryotransmission electron microscopy studies and small-angle x-ray
scattering expts., indicating the presence of multilamellar domains with a
regular spacing of 70 Å and 68 Å in BGTC/DOPE-DNA and BGTC-DNA
aggregates, resp. In addition, DNA lipoplexes with similar lamellar patterns
were detected inside transfected HeLa cells by conventional transmission
electron microscopy. These results suggest that DNA condensation by
multivalent guanidinium-cholesterol cationic lipids involves the formation
of highly ordered multilamellar domains, the DNA mols. being intercalated
between the lipid bilayers. These results also invite further

investigation of the intracellular fate of the internalized lipid/DNA structures during their trafficking toward the cell nucleus. The identification of the basic features of active complexes should indeed help in the design of improved guanidinium-based vectors.

ST supramol assembly structure guanidinium cholesterol reagent transfection
IT HeLa cell

(DNA lipoplexes with lamellar patterns detected inside transfected HeLa cells; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT DNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(condensation, by guanidinium-cholesterol cationic lipids involves formation of highly ordered multilamellar domains; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT Drug delivery systems
(liposomes, structure of lipid/DNA aggregates in; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT 2462-63-7, Dioleoyl phosphatidylethanolamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(bis(guanidinium)-tren-cholesterol with, in liposome; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT 182056-06-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

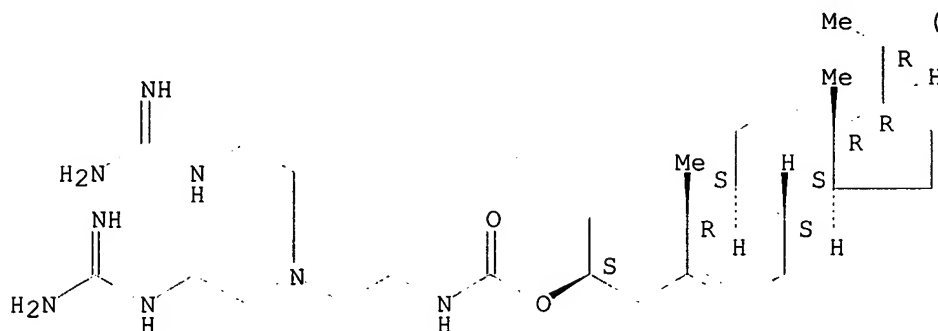
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IT 182056-06-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe₂

L34 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:687119 HCAPLUS

DN 130:57047

ED Entered STN: 30 Oct 1998

TI Guanidinium-cholesterol cationic lipids: novel reagents for gene transfection and perspectives for gene therapy

AU Oudrhiri, N.; Vigneron, J. P.; Hauchecorne, M.; Toury, R.; Lemoine, A. I.; Peuchmaur, M.; Navarro, J.; Lehn, J. M.; Lehn, P.

CS Hopital Robert Debre, INSERM U.458, Paris, 75019, Fr.

SO Biogenic Amines (1998), 14(5), 537-552

CODEN: BIAME7; ISSN: 0168-8561

PB VSP BV

DT Journal; General Review

LA English

CC 63-0 (Pharmaceuticals)

Section cross-reference(s): 1, 3

AB A review with refs. Artificial self-assembling systems are at present widely investigated as an alternative approach to recombinant viruses for gene transfer studies and gene therapy applications. Among these synthetic vectors, cationic lipids are particularly attractive as it is possible to design and synthesize a great variety of reagents. Several amine-carrying cationic lipids have been shown to be efficient for gene transfection; moreover, some reagents (DC-Chol:DOPE, DOTAP...) have even already been used in clin. trials. Over the last years, we have developed a novel class of cationic lipids : cholesterol derivs. characterized by polar head groups containing guanidinium functions. Such reagents combine the membrane compatible features of the cholesterol subunit and the favorable features of the guanidinium groups for DNA binding. We herein intend to summarize our work showing that these novel cationic lipids are efficient for gene transfection in vitro (into various mammalian cell lines and primary human airway cells) and also in vivo (into the mouse airway epithelium). These studies confirm the potential of cationic lipids for human gene therapy, namely lung-directed gene therapy for Cystic Fibrosis. Most importantly, our work also provides the basis for the design of

improved artificial gene delivery systems. Thus, in this forward-looking review, we will also discuss some of the remaining problems that need to be resolved in order to develop improved synthetic vectors for nonviral gene delivery.

ST review

IT Lipids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic; guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

IT Drug delivery systems

Gene therapy

Transformation, genetic

(guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

IT 182056-06-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 182056-06-0

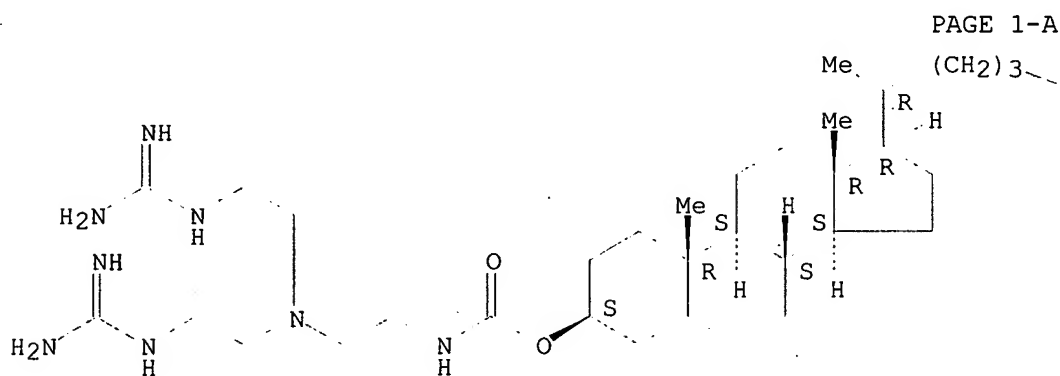
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe₂

L34 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
 AN 1997:594745 HCAPLUS
 DN 127:234484
 ED Entered STN: 17 Sep 1997
 TI Preparation of compounds related to the amidinium family and their uses in gene therapy
 IN Lehn, Jean-Marie; Lehn, Pierre; Vigneron, Jean-Pierre
 PA Centre National de la Recherche Scientifique, Fr.; Lehn, Jean-Marie; Lehn, Pierre; Vigneron, Jean-Pierre
 SO PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DT Patent
 LA French
 IC ICM C07J041-00
 ICS A61K031-575; A61K009-127; C12N015-88
 CC 32-7 (Steroids)
 Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731935	A1	19970904	WO 1997-FR364	19970228
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO,				

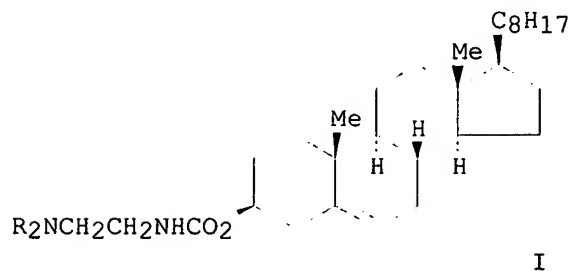
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RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

FR 2745569	A1	19970905	FR 1996-2604	19960301
FR 2745569	B1	19980507		
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FR 2751972	B1	19980904		
CA 2248186	AA	19970904	CA 1997-2248186	19970228
AU 9719304	A1	19970916	AU 1997-19304	19970228
AU 723998	B2	20000907		
EP 888379	A1	19990107	EP 1997-907154	19970228
EP 888379	B1	20010110		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
SI, FI

BR 9707889	A	20000104	BR 1997-7889	19970228
JP 2000506136	T2	20000523	JP 1997-530677	19970228
AT 198599	E	20010115	AT 1997-907154	19970228
ES 2154453	T3	20010401	ES 1997-907154	19970228
PT 888379	T	20010531	PT 1997-97907154	19970228
NO 9803691	A	19980812	NO 1998-3691	19980812
US 6143729	A	20001107	US 1998-125825	19980911
US 6316422	B1	20011113	US 2000-706619	20001106
PRAI FR 1996-2604	A	19960301		
FR 1996-9557	A	19960730		
WO 1997-FR364	W	19970228		
US 1998-125825	A1	19980911		

GI



AB . Novel amidinium derivs. R2R3NCO2R1 [R1 = cholesterol derivative, alkylamino group; R2, R3 = H, {(CH2)nNR4}mR5; R4, R5 = H, (CH2)p(X)r{(CH2)qC(NH2):N+H2}x] are disclosed. Amidine salt I·2HCl [R = (CH2)2NHC(NH2):NH] was prepd, from cholesterol chloroformate via sequential addition of tris(2-aminoethyl)amine and 1H-pyrazole-1-carboximidine. I is useful in gene therapy for transferring therapeutic genes into cells as shown by the expression of luciferase in human A549 cells (4x10⁵ RLU/mg), in monkey COS-7 cells (2.1x10⁷ RLU/mg), in dog MDCK-1 cells (3x10⁶ RLU/mg) and in rat ROS cells (4x10⁶ RLU/mg).

ST steroid amidinium deriv prepn gene therapy; cholesterol amidinium deriv prepn gene therapy

IT Amidines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

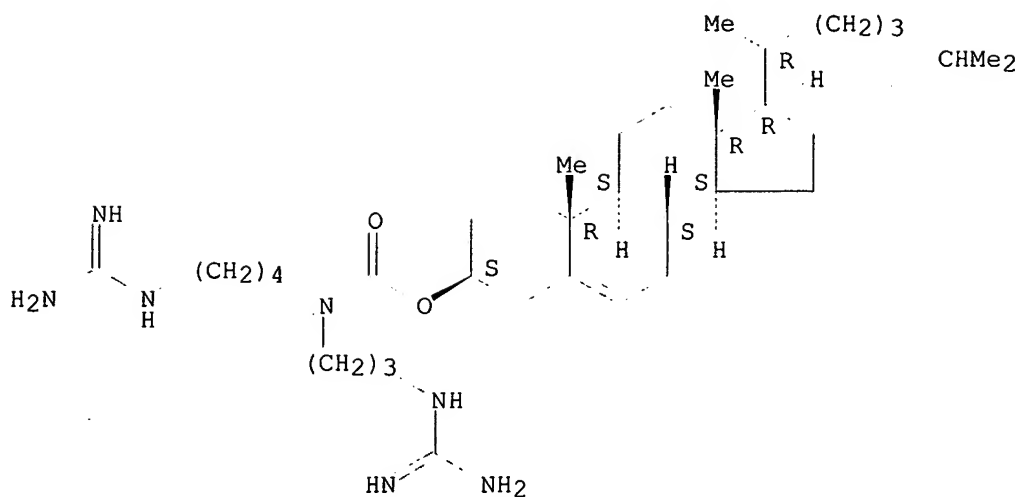
(cationic; preparation of compds. related to the amidinium family and their uses in gene therapy)

IT Gene therapy

(preparation of compds. related to the amidinium family and their uses in

- gene therapy)
- IT Steroids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- IT Liposomes
Micelles
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of compds. related to the amidinium family and their uses in gene therapy in)
- IT DNA
Plasmids
RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of compds. related to the amidinium family and their uses in gene therapy with)
- IT 182056-12-8P 182056-15-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- IT 9014-00-0, Luciferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- IT 111-94-4, Iminobis(propionitrile) 2462-63-7,
Dioleoylphosphatidylethanolamine 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 4097-89-6, TREN 7144-08-3, Cholesterol chloroformate 83392-10-3, N1,N8-Di(tert-butoxycarbonyl)spermidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- IT 179075-25-3P 195253-95-3P 195253-96-4P 195253-97-5P 195253-98-6P
195253-99-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- IT 195254-00-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- IT 182056-12-8P 182056-15-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)
- RN 182056-12-8 HCAPLUS
- CN Cholest-5-en-3-ol (3 β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

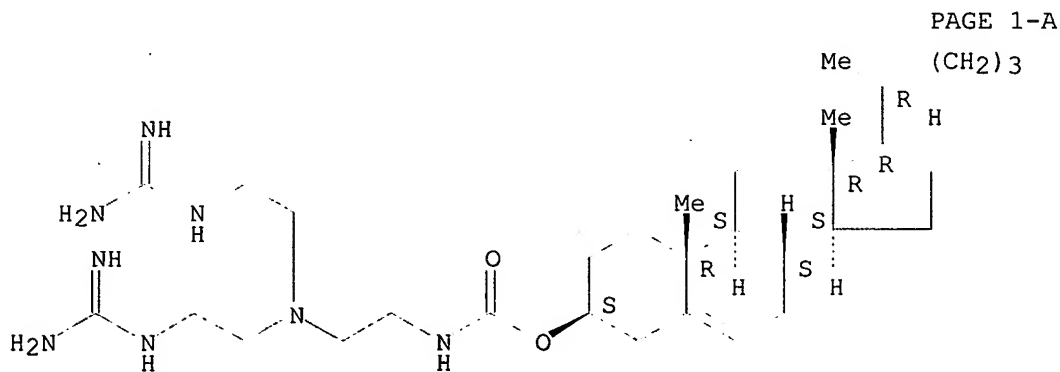


● 2 HCl

RN 182056-15-1 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

PAGE 1-B

CHMe₂

L34 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:172669 HCAPLUS

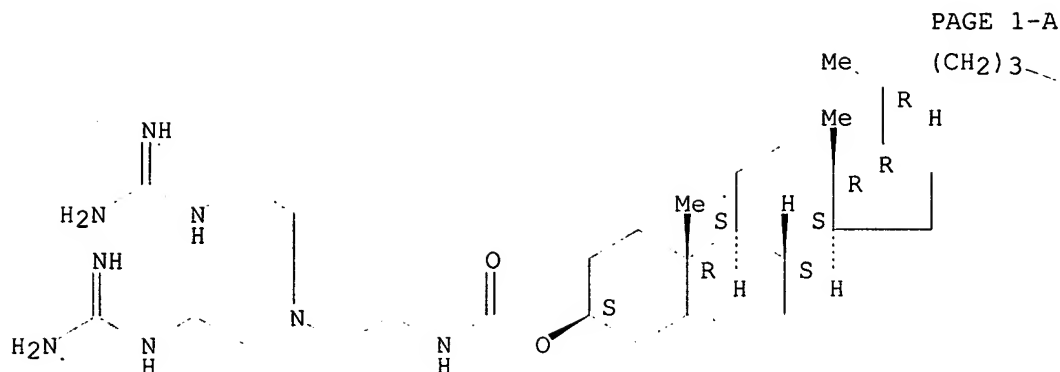
DN 126:258428

ED Entered STN: 14 Mar 1997

TI Gene transfer by guanidinium-cholesterol cationic lipids into airway

- epithelial cells in vitro and in vivo
- AU Oudrhiri, Noufissa; Vigneron, Jean-Pierre; Peuchmaur, Michel; Leclerc, Tony; Lehn, Jean-Maire; Lehn, Pierre
- CS Inst. Natl. Sante Recherche Medicale, Hopital Robert Debre, Paris, 75019, Fr.
- SO Proceedings of the National Academy of Sciences of the United States of America (1997), 94(5), 1651-1656
CODEN: PNASA6; ISSN: 0027-8424
- PB National Academy of Sciences
- DT Journal
- LA English
- CC 1-2 (Pharmacology)
Section cross-reference(s): 63
- AB Synthetic vectors represent an attractive alternative approach to viral vectors for gene transfer, in particular into airway epithelial cells for lung-directed gene therapy for cystic fibrosis. Having recently found that guanidinium-cholesterol cationic lipids're efficient reagents for gene transfer into mammalian cell lines in vitro, the authors have investigated their use for gene delivery into primary airway epithelial cells in vitro and in vivo. The results obtained indicate that the lipid bis(guanidinium)-tren-cholesterol (BGTC) can be used to transfer a reporter gene into primary human airway epithelial cells in culture. Furthermore, liposomes composed of BGTC and dioleoyl phosphatidylethanolamine (DOPE) are efficient for gene delivery to the mouse airway epithelium in vivo. Transfected cells were detected both in the surface epithelium and in submucosal glands. In addition, the transfection efficiency of BGTC/DOPE liposomes in vitro was quant. assessed by using the luciferase reporter gene system.
- ST gene transfer cationic lipid airway epithelium
- IT Respiratory tract
(epithelium; gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
- IT Gene therapy
Genetic vectors
Transduction, genetic
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
- IT Drug delivery systems
(liposomes; gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
- IT 182056-06-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into airway epithelial cells in vitro and in vivo)
- IT 4004-05-1, Dioleoyl phosphatidylethanolamine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
- IT 182056-06-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into airway epithelial cells in vitro and in vivo)
- RN 182056-06-0 HCAPLUS
- CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

CHMe₂

L34 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:553205 HCAPLUS

DN 125:239451

ED Entered STN: 17 Sep 1996

TI Guanidinium-cholesterol cationic lipids: efficient vectors for the transfection of eukaryotic cells

AU Vigneron, Jean-Pierre; Oudrhiri, Noufissa; Fauquet, Mireille; Vergely, Laurence; Bradly, Jean-Claude; Basseville, Monique; Lehn, Pierre; **Lehn, Jean-Marie**

CS Laboratoire de Chimie des Interactions Moleculaires, College de France, Paris, 75005, Fr.

SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(18), 9682-9686

CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 6

AB Two cationic lipids, bis-guanidinium-spermidine-cholesterol (BGSC) and bis-guanidinium-tren-cholesterol (BGTC)-cholesterol derivs. bearing two guanidinium groups-have been synthesized and tested as artificial vectors for gene transfer. They combine the membrane compatible features of the cholesterol subunit and the favorable structural and high pKa features of the guanidinium functions for binding DNA via its phosphate groups. Reagent BGTC is very efficient for transfection into a variety of mammalian cell lines when used as a micellar solution. In addition, both BGTC and BGSC present also a high transfection activity when formulated as liposomes with the neutral phospholipid dioleoylphosphatidyl ethanolamine. These results reveal the usefulness of cholesterol derivs. bearing guanidinium groups for gene transfer.

ST guanidinium cholesterol genetic vector transformation eukaryote

IT Eukaryote

Genetic vectors

Liposome

Transformation, genetic

(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

IT 57-88-5D, Cholesterol, guanidinium derivs.

(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

IT 182055-89-6P 182056-06-0P 182056-12-8P
182056-15-1P

IT 4023-02-3 4097-89-6 7144-08-3 83392-10-3

(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

IT 182055-89-6P 182056-06-0P 182056-12-8P
182056-15-1P

RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

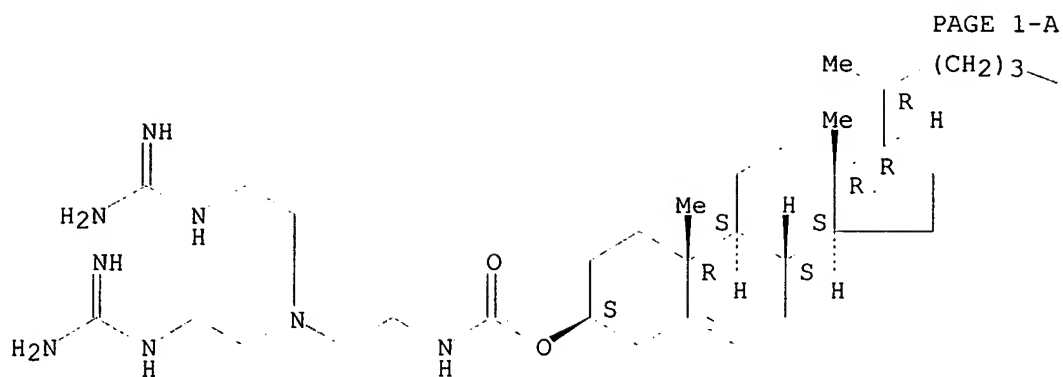
CN Cholest-5-en-3-ol (3 β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate (9CI) (CA INDEX NAME)

The chemical structure is a complex molecule consisting of several interconnected parts:

- Guanidine Group:** On the left, a guanidine moiety is shown with a central carbon double-bonded to an NH group and single-bonded to two NH₂ groups.
- Alkyl Chain:** A long alkyl chain, labeled (CH₂)₄, connects the guanidine group to a carbamate linkage.
- Carbamate Linkage:** The alkyl chain is attached to the nitrogen of a carbamate group, which is also bonded to a carbonyl oxygen and an oxygen atom.
- Thiophene Ring:** The oxygen atom of the carbamate linkage is part of a five-membered thiophene ring, which also contains a sulfur atom (S) and a methyl group (Me).
- Steroid-like Nucleus:** The thiophene ring is fused to a complex polycyclic system that resembles a steroid nucleus. This system includes several rings with methyl groups (Me) and hydrogen atoms (H) at various positions.
- Side Chain:** A side chain, labeled (CH₂)₃, is attached to the thiophene ring. This chain ends in a guanidine group, which is further substituted with an HN group and an NH₂ group.
- Other Labels:** The structure includes several other labels such as R, S, and CHMe₂, which likely represent specific stereochemical configurations or substituents.

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



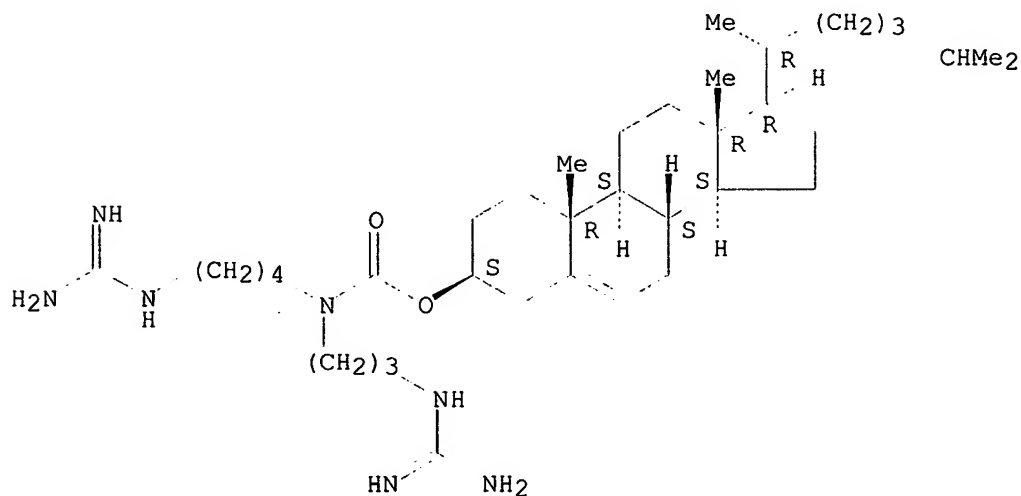
PAGE 1-B

CHMe₂

RN 182056-12-8 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



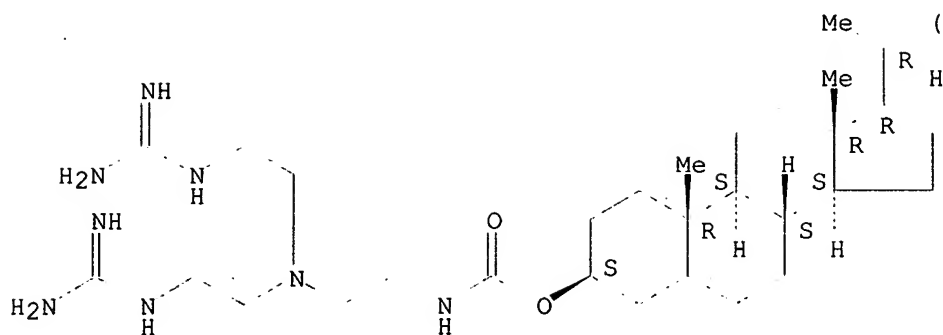
● 2 HCl

RN 182056-15-1 HCAPLUS

CN Cholest-5-en-3-ol (3 β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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(CH₂)₃

● 2 HCl

PAGE 1-B

CHMe₂

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